

**REMARKS**

This is in response to the Examiner's communication mailed July 21, 2003.

The Examiner objects to claims 87, 94, 100, 101, 119 and 120 because these claims include sequences with more than four amino acids and do not include SEQ ID NOs. The Examiner also objects to amino acid sequences in the body of the specification which do not recite SEQ ID NOs. Claims 87, 94, 100, 101, 119 and 120 have been amended to recite SEQ ID NOs. Pages 3, 4, 5 and 6 of the specification have been amended to recite SEQ ID NOs for each amino acid sequence included on these pages. In addition, claims 81 to 85, 88 to 92, 94 to 98, 100 to 106, 108 to 111 and 115 to 120 have been amended to further clarify the claims. Such amendments are fully supported by the present specification and the context of the present specification.

The Examiner objects to usage of trademarks PLURONIC and TYLOXAPOL on page 19 of the specification indicating that the trademarks should be capitalized whenever appearing in the specification and should be accompanied by generic terminology. Applicant disagrees with the Examiner in part.

Pluronic is preceded by a generic description of the composition and is followed by ®, clearly indicating that Pluronic is a trademark. The trademark "Tyloxapol" is preceded by a generic description of the composition. Applicant has amended the specification to include "®" after "Tyloxapol." Applicant believes that placing a "®" after a trademark is an appropriate way to indicate a trademark. This is supported by MPEP 608.01(v) which states that each letter of the trademark word should be capitalized or a proper trademark symbol such a ® or ™ should follow the word. Applicant has also included ® after "Tween" on page 19.

Claims 82, 89, 96, 102, 108 and 114 have been rejected under 35 U.S.C. 112, second paragraph as being indefinite for failing to

particularly point out and distinctly the subject matter which applicant regards as the invention. In particular, the Examiner states that the phrase "less than about" is indefinite. Applicant traverses this rejection.

Applicant believes that claims 82, 89, 96, 102, 108 and 114 as originally filed make clear and definite the subject matter for which applicant seeks patent protection. For example, the terms "less than" and "about" as used together in the present claims are not inconsistent. To reject the present claims alleging that "less than about" is indefinite, the Examiner is attempting to place an unjustified and improper restriction on the scope of the present claims. However, in the interest of facilitating prosecution of the present patent application, applicant has amended claims 82, 89, 96, 102, 108 and 114, to state that the component "is present in an effective amount less than about ...". An effective amount cannot be an amount less than 0%. Applicant submits that these amendments comply with the Examiner's comments regarding the subject matter of claims 82, 89, 96, 102, 108 and 114 and that, therefore, the present rejection should be withdrawn.

The Examiner has rejected one or more pending independent claims 81, 88, 95, 101, 106 and 113 as being anticipated by Huth et al (WO 96/25183), by Hunt (US Patent No. 5,549,849) and/or by Maloy (US Patent No. 5,792,831), each under 35 U.S.C 102(b). The Examiner has also rejected independent claim 95 as being anticipated by Deckers et al (US Patent No. 6,372,234) under 35 U.S.C. 102(e). Applicant traverses each of these rejections.

The Examiner has rejected claims 81 to 86, 106 and 108 to 118 as being anticipated by Huth et al. Huth et al does not specifically disclose the present invention. The Examiner states that Huth et al discloses an antimicrobial agent present in a therapeutically effective amount, thereby anticipating claim 81, pointing to page 12, line 25 to 29 of the Huth et al reference. At

this point, Huth et al states that non-oxidative antimicrobial components may be present in "the range of about 0.000005% or about 0.00001% to about 2% (w/v)." There is no statement indicating that the antimicrobial components are useful in a therapeutically effective amount. Even if compositions of Huth et al disclosed an antimicrobial peptide present in a therapeutically effective amount, claim 81 of the above-identified application recites that the composition further includes an effective amount of a therapeutically effective component, that is a therapeutically effective component in addition to an antimicrobial peptide preservative. Huth et al does not specifically disclose, teach or suggest this feature of the present invention.

The Examiner indicates that claim 12 of Huth et al anticipates pending claim 106. Pending claim 106 states that the composition is applied onto or into the eye. Claim 12 of Huth et al states: "placing said contact lens directly from said liquid medium into a mammalian eye." Claim 12 of Huth et al is not directed to placing a composition in the eye. Rather, claim 12 of Huth et al is directed to treating a contact lens and thereafter placing the lens into the eye.

Pending claim 113 includes the feature of an antimicrobial peptide mimetic. The Examiner states that claim 21 of Huth et al anticipates pending claim 113. However, nowhere in claim 21 of Huth et al is an antimicrobial peptide mimetic specifically disclosed or suggested.

In view of the above, applicant submits that the present claims, and in particular claims 81 to 86, 106 and 108 to 118, are not anticipated by and are unobvious from and patentable over Huth et al under 35 U.S.C. 102(b) and 103.

The Examiner has rejected claims 81 to 83 and 88 to 93 as being anticipated by Hunt. Hunt discloses compositions useful for treating a contact lens. Hunt does not specifically disclose the

present invention. For example, Hunt does not specifically disclose, teach or suggest compositions which include an antimicrobial peptide present in an amount effective as a preservative and further includes an effective amount of a therapeutically effective component in addition to the preservative, as recited in independent claim 81. Moreover, Hunt does not specifically disclose, teach or suggest a component selected from magainin antimicrobial peptides, analogs thereof and mixtures thereof as a sole preservative in a composition, as recited in independent claim 88. The Examiner points to column 9, lines 10 to 11 for support in showing that Hunt discloses ophthalmic compositions comprising one active agent. It is stated in column 9, lines 10 to 11 that "the present invention can include treatment with both the D-enantiomeric anti-microbial agent(s) alone and with a ...". The language cited by the Examiner does not refer to a component selected from magainin antimicrobial peptides, analogs thereof and mixtures thereof. Further, the language does not specify use of an individual antimicrobial agent.

In addition, Hunt discloses ophthalmic compositions in which antimicrobial peptides are useful as disinfectants. A composition which is preserved using a certain substance is not the same as a composition which is disinfecting using the same substance. A preserved composition is a composition in which microbial population growth is substantially prevented. A disinfecting composition is effective to reduce the population of microbial organisms, for example, when applied to a solid surface, such as a contact lens.

In view of the above, applicant submits that the present claims, and in particular claims 81 to 83 and 88 to 93, are not anticipated by and are unobvious from and patentable over Hunt under 35 U.S.C. 102(b) and 103.

The Examiner has rejected claims 81, 84 to 88, 91 to 94, 101,

104 to 106 and 110 to 112 as being anticipated by Maloy. Maloy discloses certain analogs of magainin peptides. The Examiner points out that Maloy states "The peptides are also useful in the prevention or treatment of eye infections" (Column 19, lines 27 to 28).

Maloy does not disclose, teach or suggest the present invention. For example, Maloy does not disclose, teach or even suggest ophthalmic compositions which include an effective amount of a component selected from magainin antimicrobial peptides, analogs thereof and mixtures thereof as a preservative and further including an effective amount of a therapeutically effective component, as recited in claim 81.

The Examiner points to column 28, lines 48 to 50, and Example 1 of Maloy stating that use of a magainin as a sole preservative is disclosed, thereby anticipating claim 88. At this point, Maloy states "Because of the antibiotic properties of the peptides, they may also be used as preservatives or sterilants of materials susceptible to microbial contamination." This passage of Maloy, does not disclose, teach or even suggest the use of an antimicrobial peptide, let alone one or more magainin antimicrobial peptides and/or analogs thereof, as a sole preservative in a composition, in particular in an ophthalmic composition, as recited in independent claim 88.

The Examiner states that Maloy discloses a sequence identical to SEQ ID NO: 4 of the above-identified application in distilled water, thereby anticipating claim 101. Distilled water is not an ophthalmic composition as is understood by a person of ordinary skill in the art. Maloy does not disclose, teach or even suggest ophthalmic compositions. Therefore, Maloy does not disclose, teach or even suggest an ophthalmic composition comprising an antimicrobial peptide of SEQ ID NO: 4, as in pending claim 101.

The Examiner points to column 29, lines 27 to 28 of Maloy,

stating that disclosed therein is an ophthalmic composition that is applied topically onto the eye. Column 29, lines 27 to 28 of Maloy, states "The peptides are also useful in the prevention or treatment of eye infections. ..." There is no indication that the peptides are applied to the eyes. "Treatment" may be accomplished by any number of methods of administration, including, but not limited to, systemic administration such as oral or intravenous administration. Maloy does not disclose, teach or even suggest application of an ophthalmic composition into or onto the eye, as in pending claim 106.

In view of the above, applicant submits that the present claims, and in particular claims 81, 84 to 88, 91 to 94, 101, 104 to 106 and 110 to 112, are not anticipated by and are unobvious from and patentable over Maloy under 35 U.S.C. 102(b) and 103.

The Examiner has rejected claims 95, 98 and 99 as being anticipated by Deckers et al. The Examiner states that the oil-in-water emulsions of Deckers anticipate independent claim 95.

Deckers et al relates to certain emulsion formulations useful for topical application to the skin. The Examiner points to column 22, lines 8 to 22 in Deckers et al which states "Proteins and peptides which may be used in accordance with the present invention include ... antimicrobial peptides such as magainin ...".

Deckers et al does not disclose, teach or suggest the present invention. For example, Deckers et al does not disclose, teach or even suggest that magainin peptides are useful as preservatives. Moreover, Deckers et al provides no disclosure, and provides no motivation to one of ordinary skill in the art, to prepare disclosure included an ophthalmic composition which includes a magainin as a preservative.

The Examiner points to column 24, lines 43 to 44 of Deckers et al, which discloses that the compositions of Deckers et al can be used as an eye make-up remover. Applicant submits that eye make-up

remover is not an ophthalmic composition as that term is used in the art. Eye make-up removers are applied to the eyelid or other skin around the eye; but, are not intended to be applied to the eye, as is an oil-in-water emulsion ophthalmic composition, as recited in independent claim 95.

In view of the above, applicant submits that the present claims, and in particular claims 95, 98 and 99, are not anticipated by and are unobvious from and patentable over Deckers et al under 35 U.S.C. 102(e) and 103.

The Examiner rejects claims 81, 84 to 88, 91 to 95, 98, 99, 101, 104 to 106 and 110 to 112 as obvious over Maloy in view of Stevenson et al under 35 U.S.C. 103(a). Claims 81, 84 to 88, 91 to 105, 110 to 112, 119 and 120 have been rejected as obvious over Maloy in view of Stevenson et al and further in view of Hunt under 35 U.S.C. 103(a). Applicant traverses each of these rejections.

Stevenson et al discloses topical application of cyclosporin A as a treatment for dry eye.

To establish a prima facie case of obviousness, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify a primary reference or to combine teachings from two or more references (MPEP § 2143).

Nowhere in Maloy, Stevenson et al or Hunt et al is there provided any motivation (either implicit or explicit) to combine the teachings and/or suggestions from any of these references, let alone to do so and obtain the present invention. To the contrary, each of these references relates to substantially different subject matter. Stevenson et al relates to application of cyclosporin A; Hunt discloses ophthalmic compositions in which antimicrobial peptides are useful as disinfectants; and Maloy relates specifically to certain analogs of magainin peptides. Applicant submits that, absent hindsight knowledge of applicant's disclosure

and invention, one of ordinary skill in the art is provided with no motivation or incentive to combine the teachings of these diverse references for any purpose, let alone for the purpose of obtaining the present invention. It is improper to rely on hindsight knowledge of applicant's invention and disclosure to reject patent claims.

In view of the above, applicant submits that the present claims, and in particular claims 81, 84 to 88, 91 to 106, 110 to 112, 119 and 120, are unobvious from and patentable over Maloy, Stevenson et al and Hunt, and any combination thereof, under 35 U.S.C. 103(a).

The Examiner rejects claims 106 to 109 as obvious over Kross (US Patent No. 5,993,864) in view of Malloy, each under 35 U.S.C. 103(a). Applicant traverses this rejection.

Maloy and Kross, alone or in combination, do not disclose, teach or suggest the present invention. As discussed above, to establish a prima facie case of obviousness, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify a primary reference or to combine teachings from two or more references (MPEP § 2143).

Kross discloses chelate complexes useful for the formation of stable molecular chlorine dioxide. Maloy discloses certain analogs of magainin peptides. Nothing contained in Kross and Maloy would provide any motivation or incentive to one of ordinary skill in the art to combine these references for any purpose, or suggest to a practitioner of ordinary skill in the art a desirability of combining these two references, let alone to do so and obtain the invention recited in claims 106 to 109.

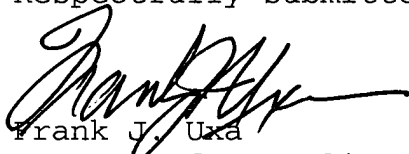
In view of the above, applicant submits that the present claims, and in particular claims 106 to 109, are unobvious from and patentable over Kross in view of Maloy under 35 U.S.C. 103(a).



Each of the present dependent claims is separately patentable over the prior art. For example, none of the prior art disclose, teach or even suggest the present compositions and methods including the additional feature or features recited in any of the present dependent claims. Therefore, applicant submits that each of the present claims is separately patentable over the prior art.

In conclusion, applicant submits that all of the present claims, that is claims 81 to 120, are allowable and respectfully requests the Examiner to pass the above-identified application to issuance at an early date. Should any matters remain unresolved, the Examiner requested to call (collect) applicant's attorney, telephone number given below.

Respectfully submitted,



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